wherein said target receptors bonded with a single carrier particle have the same or different base sequences;

and

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the second end of each receptor, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances;

wherein the number and length of target receptors bonded to said carrier particle is such that a major influence by energy movement or quenching among the labeled substances does not occur, thereby enhancing discrimination by stable emission.

36. (New) A labeled complex, comprising:

a carrier particle selected from the group consisting of a magnetic particle, charged particle, dielectric, chemotactic microorganism, synthetic resin bead, latex particle, glass bead, gel substance, and a metallic particle;

a number of target receptors of length up to 1mm, wherein said target receptors are double stranded nucleic acids of predetermined base sequence, each double stranded nucleic acid having a first single strand and a second single strand, each single strand having a first and a second end, wherein the target receptor has a first end of a first single strand bonded with said carrier, and wherein said target receptors bonded with a single carrier particle have the same or different base sequences;

and

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the second end of a second single strand, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances;

wherein the number and length of target receptors bonded to said carrier particle is such that a major influence by energy movement or quenching among the labeled substances does not occur, thereby enhancing discrimination by stable emission.

37. (New) A labeled complex, comprising:

a carrier particle selected from the group consisting of a magnetic particle, charged particle, dielectric, chemotactic microorganism, synthetic resin bead, latex particle, glass bead, gel substance, and a metallic particle;

a number of target receptors of length up to 1mm, wherein said target receptors are double stranded nucleic acids having a predetermined base sequence, each double stranded nucleic acid having a

first single strand and a second single strand, each single strand having a first and a second end, wherein the target receptor has a second end of a first single strand bonded with said carrier, wherein said target receptors bonded with a single carrier particle have the same or different base sequences;

and

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the first end of a first single strand, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances;

wherein the number and length of target receptors bonded to said carrier particle is such that a major influence by energy movement or quenching among the labeled substances does not occur, thereby enhancing discrimination by stable emission.

REMARKS

I. Status of the Application

Claims 1- 7 are canceled. Nonelected Claims 12-34 are canceled without prejudice for filing divisional applications. Claims 8-11 are amended. Claims 35-37 are added and correspond to the elected species. Claims 8-11 and 35-37 are pending.

II. Support for Amended and Added Claim Language

Amended and added claim language has support in the specification and drawings as follows:

Claim 8:

"first and second labeled substances" has support at page 25, lines 1-2;

Claim 11:

"wherein said carrier is a magnetic particle" has support at page 13, line 5, and in claims as originally filed;

Claim 35:

"a carrier particle selected from the group consisting of a magnetic particle, charged particle, dielectric, chemotactic microorganism, synthetic resin bead, latex particle, glass bead, gel substance, and a metallic particle" has support at page 12, lines 26-27, and at page 5, lines 14-15;

"a number of target receptors of length up to 1mm, each receptor having a first end and a second end" has support at page 7, lines 18-24; page 5, lines 11-13, and claims as originally filed;

"wherein the first end of each receptor is bonded with said carrier particle" has support at page 7, lines 21-23;

"wherein said target receptors are single-stranded nucleic acids of predetermined base sequence" has support at page 11, lines 12-13;

"wherein said target receptors bonded with a single carrier particle have the same or different base sequences" has support in claim 1 as originally filed and page 7, lines 14-17, where a plurality of types of target per carrier is described;

"at least a first type and a second type of labeled substance" has support at page 24, lines 16-18;

"each labeled substance bonded to a fraction of the number of target receptors at the second end of each receptor, thereby forming a labeled complex having a predetermined molar ratio of the labeled substances" has support at page 25, lines 1-3;

"wherein the number and length of target receptors bonded to said carrier particle is such that a major influence by energy movement or quenching among the labeled substances does not occur, thereby

enhancing discrimination by stable emission" has support at page 6, lines 17-23; page 8, lines 16-21, and page 28, lines 14-19.

Claim 36:

"wherein said target receptors are double stranded nucleic acids of predetermined base sequence, each double stranded nucleic acid having a first single strand and a second single strand, each single strand having a first and a second end, wherein the target receptor has a first end of a first single strand bonded with said carrier" has support at page 10, lines 18-22, and claims as originally filed;

Claim 37:

"wherein said target receptors are double stranded nucleic acids having a predetermined base sequence, each double stranded nucleic acid having a first single strand and a second single strand, each single strand having a first and a second end, wherein the target receptor has a second end of a first single strand bonded with said carrier" has support at page 11, lines 3-7, and claims as originally filed.

The amended claim language and added claim language clarify the invention in light of the written description rejections. When read in light of the specification, and the restriction and election requirement, no narrowing of an element of the pending claims was believed made. No new matter has been introduced by the amendments to the claims or by the added claims.

III. Rejection of the Title of the Invention

Office Action

The Office Action stated that the title of the invention is not descriptive.

Response

The title of the invention has been amended.

IV. Objection to Claims 4-11

Office Action

Claims 4-11 were objected to as being improperly dependent and as encompassing non-elected embodiments.

Response

Claims 4-7 have been canceled and replaced with added claims. Claims 8-11 have been amended to be properly dependent and to recite elected embodiments.

V. Rejections of Claims 1-3 under §112, First Paragraph

Office Action

Claims 1-3 were rejected for lacking description for claimed genera, lacking a restriction on length, on heterogeneity/similarity, on the number of polynucleotides immobilized on the carrier, and lacking specific starting materials and reaction conditions. The specification was cited as lacking teachings on how to make and use the claimed invention. Schleifer, U.S. Patent 6,077,674, and Carrico, U.S. Patent 5,200,313, were cited for identifying problematic aspects of manufacture of oligonucleotide arrays and of hybridization reactions, respectively.

Response

Claims 1-3 are canceled. Pending claims address these rejections as follows:

"lacking description for claimed genera": The presently elected invention relates to properties common to nucleic acids in general. For example, linear nucleic acids have 3' and 5' ends, they contain sugars and phosphate bonds. Nucleic acids hybridize to their complementary strand by well known rules. Nucleic acids bind proteins that have binding specificity for a particular sequence of the nucleic acid under conditions readily determined by one of skill in the art. The present invention provides a labeled complex that includes nucleic acids and relies on those general properties of nucleic acids that are common to nucleic acids. A requirement for a specific genus or species of nucleic acid or specific sequences of nucleic acid is simply not applicable to the present invention.

"no restriction on length": The claims recite that the target receptors have a length of up to 1mm.

"no restriction on heterogeneity/similarity": The claims recite that the target receptors bonded with a single carrier particle have the same or different base sequences.

"no restriction on the number of immobilized polynucleotides that are immobilized to the carrier": The claims recite that the number and length of target receptors (nucleic acids) bonded to the carrier particle is such that a major influence by energy movement or quenching among the labeled substances does not occur, thereby enhancing discrimination by stable emission.

"lacking specific starting materials and reaction conditions": An example of starting materials is provided in Fig. 1 and the description thereof at page 24, line 13 to page 25, line 12 where a magnetic particle is provided as a carrier particle, DNA fragments with a predetermined base sequence as target receptors, and FITC, rhodamine, or Cy5 as labeled substances. The target receptors are bonded to the magnetic particle by a bond of biotin and avidin. Individual reaction conditions for coupling a particle to avidin, for coupling a nucleic acid to biotin, and for coupling a nucleic acid to FITC, rhodamine, or Cy5 are known to one of ordinary skill in the art in light of the specification. *Lindemann v. American Hoist*, 221 USPQ 481 (Fed. Cir. 1984) states: "The question is whether the disclosure is sufficient to enable those skilled in the art to practice the claimed invention, hence the specification need not disclose what is well known in the art." Further, Staehelin v. Secher, 24 USPQ 2d 1513 (B.P.A.I. 1992) states: "In satisfying the enablement requirement, an application need not teach, and preferably omits, that which is

well-known in the art. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986); and *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). How such a teaching is set forth, whether by the use of illustrative examples or by broad descriptive terminology, is of no importance since a specification which teaches how to make and use the invention in terms which correspond in scope to the claims *must* be taken as complying with the first paragraph of 35 USC 112 *unless* there is reason to doubt the objective truth of the statements relied upon therein for enabling support. *Marzocchi* at 439 F.2d 223, 169 USPQ 369."

"lacking teachings on how to make and use the claimed invention": Applicants respectfully submit that the specification teaches one of ordinary skill in the art how to make and use the claimed invention without undue experimentation. In particular the figures and description thereof at pages 24 to 38 provide enablement of the invention. In addition, Fig. 10 and description thereof at pages 39-43 set forth a process for utilizing a labeled complex of the invention.

The fact that the specification is devoid of a working example is without significance. Examples are not necessary. While a full example may have provided additional useful information, one possessed of the knowledge of one skilled in this art could practice the invention without the exercise of an undue amount of experimentation. *Ex parte Nardi and Simier*, 229 USPQ 79 (BPAI 1986).

Regarding Schleifer '674: While the length of oligonucleotides of oligonucleotide arrays made using step-by-step in situ synthesis is limited by the efficiency of each chemical coupling reaction, the presently claimed invention is not so limited. Target nucleic acid receptors may be isolated from nature, may be restriction fragments, PCR products, or the product of polymerization using a DNA synthesis enzyme, for example.

The application underlying Carrico '224 is the culmination of continuation and continuation-in-part applications having filing dates ranging from 1983 to 1985. U.S. Patent No. 5,780,224 to Collins, cited in the 102(b) rejection infra, provides evidence that one of ordinary skill in the art as of 1986 could overcome Carrico's concerns. Specifically, Collins '224 which issued from an application that was the culmination of a chain of continuation applications first filed in 1986, claims a method for assaying a sample for target nucleic acid using hybridization techniques. In addition, the applications underlying Carrico '224 were filed 13 and 15 years prior to the priority date of the present application. The art of hybridization improved substantially by 1998, the priority date of the present application. No more than routine experimentation is needed to practice the claimed subject matter in light of the present specification.

VI. Rejection of Claims 1-3 under §112, Second Paragraph

Office Action

Claims 1-3 were rejected for the terms "large," "substantially," and "slender."

Response

Claims 1-3 are canceled. The pending claims do not recite the cited terms.

VII. Rejection of Claims 1-3 under §102(b)

Office Action

Claims 1-3 were rejected as anticipated by Collins, U.S. 5,780,224.

Response

Claims 1-3 are canceled. Applicants therefore respectfully request that the rejection under 102(b) be withdrawn.

VIII. Collins, U.S. 5,780,224 With Respect to Added Claims 35-37

With respect to added Claims 35-37, Collins '224 does not teach or suggest the element of "at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the second end of each receptor, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances." While Collins teaches a second probe having at least one label moiety capable of detection (col. 12, line 36), and teaches ^{32}P-dCTP and ^{32}P-dGTP (col. 22, line 28), Collins does not teach "at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the second end of each receptor, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances."

For a prior art reference to anticipate in terms of 35 U.S.C. §102, every element of the claimed invention must be identically shown in a single reference. *In re Bond* (CAFC) 15 USPQ2d 1566, 1990. Further, regarding an obviousness rejection, the Federal Circuit has required that specific support must be found in the prior art that "suggests" or "teaches" the modification necessary to resolve the differences of the prior art with a claimed invention. *In re Grabiak*, 226 USPQ 870 (Fed. Cir. 1985).

For the reasons stated above, Applicants submit that Collins '224 does not anticipate the presently claimed invention, and that Collins '224 does not render obvious the presently claimed invention since no suggestion is provided to resolve the differences of Collins '224 and the presently claimed invention.

IX. Conclusion

It is believed that all matters set forth in the Office Action have been addressed. Reconsideration and an early indication of the allowability of the pending claims are respectfully requested. Should the

Examiner believe that an interview with Applicant's undersigned agent would expedite consideration of the pending claims, the Examiner is invited to call the undersigned agent at the telephone number indicated below.

Respectfully submitted,

Gloria L. Norberg

Dated: July 10, 2003

Gloria L. Norberg
Registration No. 36,706
HAYNES AND BOONE, LLP
901 Main Street - Suite 3100
Dallas, Texas 75202-3789
Telephone: 512.867.8528
Facsimile: 512.867.8632
File: 10287.39